REMARKS

This Substitute Amendment and Response is being filed as an accommodation to the Examiner stemming from a telephone discussion between the Examiner and the undersigned on October 22, 2007. During that discussion the undersigned pointed out that the October 2, 2007 "communication" of a "not fully responsive reply" was not appropriate, *inter alia*, because the Examiner's asserted "withdrawal" of claims 5-7 without a restriction requirement was without any support in the rules or the law. The undersigned therefore requested that the Examiner withdraw the "communication" and act on Applicant's July 27, 2007 Amendment and Response. The Examiner declined, and in the ensuing discussion the undersigned undertook, as a courtesy to the Examiner, to file this substitute Amendment and Response in lieu of a petition.

The above amendments build on original method claim 4, which original claim was in proper method format (it was not in a "use" format, contrary to the Examiner's assertion), did not have improper multiple dependency, and was treated on the merits by the Examiner in the October 10, 2006 Action. All other claims have been cancelled. As detailed below, starting with this proper original method claim 4, the above amendments add limitations from the specification that directly address the grounds for rejection, and remove terms that were objected to by the Examiner. It is therefore not seen how this substitute Amendment and Response could in any way be considered "not fully responsive." However, should the Examiner nevertheless find the present substitute Amendment and Response to be "not fully responsive," Applicant reserves the right to petition the "communication" or take what other recourse was available to it, had this accommodation not been made.

Reconsideration of the May 2, 2007 rejection of all claims is therefore respectfully requested in view of the above amendments and the following remarks.

Amendment of Title of Invention

The Title of the Invention has been amended to correct an obvious typographical error, simply changing "OF" to "OR", so that the Title reads the same as the title of the published PCT application, of which the present application is the US National Stage.

Claim Amendments

Claims 1, 2 and 3 have been cancelled as being in a "use" format not generally accepted under US practice.

Claims 5-7 have been cancelled, in order to expedite the prosecution of this application, in view of the Examiner's assertion that these claims have been "withdrawn," without acknowledging the correctness of such assertion and/or such withdrawal.

Remaining **method of treatment claim 4** has been amended to address the specific points of rejection of this claim, as detailed further below. Specification support for the amendments to claim 4 is as follows:

- Support for replacing "constipation" with "functional constipation or C-IBS" is found in the specification at page 4, lines 20-21, where it is stated, "[h]erein where the term 'constipation' is used, it is to be understood that this term, unless otherwise qualified, relates to functional constipation and C-IBS." Inasmuch as the term "constipation" is *not* "otherwise qualified" in claim 4, this substitution of "functional constipation or C-IBS" for the term "constipation" does not change the scope of this claim.
- Support for the listing of specific IBAT inhibitor compounds is found at specification page 11, line 10 through page 12, line 13, with this specific compound listing also being found verbatim in original claim 7.
- Support for replacing the term "or a prodrug" with "or an *in vivo* hydrolysable ester formed on an available carboxy or hydroxy or an *in vivo* hydrolysable amide formed on an available carboxy" is found in the specification at page 26, lines to 31.
- The deletions of "prophylaxis" and "such as man" address specific grounds for objection and/or rejection asserted by the Examiner.

New claim 8 has been added to further limit the method of claim 4 to the treatment of functional constipation. Specification support for this claim is found, *inter alia*, at page 4, lines 21-23, and also in original claim 5.

New claim 9 has been added to further limit the method of claim 4 to the treatment of C-IBS. Specification support for this claim is found, *inter alia*, at page 4, lines 21-23, and

also in original claim 6 ("C-IBS" being "constipation predominant irritable bowel syndrome; see, *e.g.*, specification page 1, line 2).

These amendments are being made without waiver or prejudice to Applicant's right to prosecute any subject matter deleted thereby in one or more continuing applications.

It should be apparent from the above that no new matter has been added, and therefore entry of these amendments is believed to be in order and is respectfully requested. Following entry of these amendments, claims 4, 8 and 9 remain pending in this application.

Objection to Abstract

At page 2 of the Action, the Abstract of the disclosure is objected to because it is not drawn to the subject matter currently under consideration. A substitute Abstract has been provided on a separate page which it is believed overcomes this objection.

Claim Rejections - 35 USC § 112, 2nd Paragraph

At page 2 of the Action, claims 1, 3 and 4 are rejected under 35 U.S.C. 112, second paragraph as being indefinite with respect to the recitation of "such as man." This rejection of claims 1 and 3 has been obviated by the cancellation of these claims, and this ground for rejection of claim 4 has been overcome by the deletion of the term "such as man" from claim 4 by the above amendments. It is therefore respectfully requested that this ground for rejection be withdrawn.

At page 2 of the Action, claims 1 and 4-7 are rejected under 35 U.S.C. 112, second paragraph as being indefinite for being in a "use" format. This rejection of claims 1 and 5-7 has been obviated by the cancellation of these claims. It is respectfully submitted that claim 4 as originally submitted was in a proper method of treatment form (not a "use" format), and claim 4 as amended above remains in a proper method of treatment form. It is therefore respectfully requested that this ground for rejection be withdrawn.

Claim Rejections - 35 USC §101

At pages 2-3 of the Action, claims 1 and 4-7 are rejected under 35 U.S.C. 101 "because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101." This rejection of claims 1 and 5-7 has been obviated by the cancellation of these claims. However, it is respectfully submitted that claim 4 as originally submitted was in a proper process (method of treatment) form (not a "use" format), and it recited the process step of "*administering* to said animal an effective amount of an IBAT inhibitor." Claim 4 as amended above remains in a proper process (method of treatment) form. It is therefore respectfully submitted that this ground for rejection with respect to claim 4 was in error, and that this ground for rejection should be withdrawn.

Claim Rejections - 35 USC § 112, 2nd Paragraph

At pages 3-4 of the Action, claims 1, 2 and 4 are rejection under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement in relation to the term "or a prodrug thereof" with respect to an IBAT inhibitor. This ground for rejection with respect to claims 1 and 2 has been obviated by the cancellation of these claims.

With respect to this ground for rejection of method claim 4, Applicants respectfully disagree, as the term "prodrug" in relation to the disclosed IBAT inhibitors is specifically described in the specification at page 26, lines 7-31. Nevertheless, in order to expedite the prosecution of this application to allowance, the term "prodrug" has been replaced in independent claim 4 by the more specific definition thereof, being "an *in vivo* hydrolysable ester formed on an available carboxy or hydroxy or an *in vivo* hydrolysable amide formed on an available carboxy thereof." Clear support for this recitation is found in the specification at page 26, lines 7-31, and a number of suitable esters that can be formed on available carboxy or hydroxy groups of the compounds recited in claim 4, as well as a number of suitable amides that can be formed on available carboxy groups of such compounds, are specifically listed in this portion of the specification. It is respectfully submitted that such *in vivo* hydrolysable esters and amides are clearly "described" as a part of Applicants' invention, and

persons skilled in this art would be enabled to select and make suitable such esters and amides, particularly in view of the very specific guidance in the specification as noted above. It is therefore submitted that the amendment to the claim 4 has overcome this ground for rejection, and it is respectfully requested that this ground for rejection be withdrawn.

At pages 4 *et seq.* of the Action, claim 4 has been rejected under 35 U.S.C. 112, first paragraph, with respect to "scope of enablement." The Examiner asserts that "the specification, while being enabling for showing that various benzothiadiazepines treat constipation in an animal model, does not reasonably provide enablement for prevention of constipation from any cause or etiologic factor." It is respectfully submitted that this ground for rejection has been overcome by the above amendments to claim 4. As now amended, independent claim 4 is directed toward a method of treatment of "functional constipation or C-IBS" in a warm-blooded animal which comprises administering to said animal an effective amount an IBAT inhibitor selected from the specific benzothiadiazepine compounds listed in claim 4. Specification support for these amendments is noted at page 8 of this substitute Amendment and Response.

As noted above, the term "constipation" is clearly defined at specification page 4, lines 20-21 as meaning "functional constipation and C-IBS." Nevertheless, in order to expedite the prosecution of this application, claim 4 now specifically recites "functional constipation or C-IBS." The scope and meaning of each of these terms is described in the specification, and in particular is defined according to "Rome 2 Criteria" (Gut 45 (Suppl 2): 43, 1999, II43-II47 (see specification page 4, lines 30-32).

Additionally, claim 4 is now directed toward the "treatment" of functional constipation and C-IBS. The recitation of "prophylaxis" is believed to be unnecessary inasmuch as the ordinary meaning of the term "treatment" would encompass the administration of the claimed therapy to patients who have had indications of constipation, in order to maintain regularity over a period of time. The term "prophylaxis" has therefore been removed from the claims in order to expedite the prosecution of this application.

In view of the above amendments and discussion, it is respectfully submitted that the skilled person would be fully enabled by the specification (without undue experimentation) to carry out the "treatment" of "functional constipation or C-IBS" by administration of a

compound that is specifically itemized in claim 4. It is therefore respectfully submitted that independent claim 4 and dependent claims 8 and 9 are fully enabled by the specification, and withdrawal of this ground for rejection is therefore appropriate.

Claim Rejections - 35 USC § 102(e)

At pages 7-8 of the Action, claims 1-4 are rejected under 35 U.S.C. 102(e) as being anticipated by Lindquist, A-M, US 2005/0124557. This ground for rejection with respect to claims 1-3 has been obviated by the cancellation of these claims. Moreover, it is respectfully submitted that the fact that claim 4 is now directed toward the administration of the specific compounds recited therein fully distinguishes claim 4 (and thus necessarily dependent claims 8 and 9) from the Lindquist reference, which does not disclose any of such compounds. Lindquist, at best, mentions only a theory that compounds having an IBAT inhibitory effect might have a laxative effect, rather than promoting constipation, when administered for treating hypercholesterolemia. Accordingly, it is respectfully requested that this ground for rejection be withdrawn.

Conclusion

All grounds for objection and or rejection having been fully addressed by the above amendments and remarks and overcome, it is believed that each of presently pending claims 4 and 8-9 is now in condition for allowance, and a Notice to that effect is respectfully requested. However, if there are any questions or remaining issues that need to be resolved before allowance, it is suggested that the Examiner telephone the undersigned to see if their resolution can be expedited.

EXCEPT for issue fees payable under 37 C.F.R. § 1.18, the Director is hereby authorized by this paper to charge any additional fees during the entire pendency of this application including fees due under 37 C.F.R. §§ 1.16 and 1.17 which may be required,

including any required extension of time fees, or credit any overpayment to Deposit Account 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully Submitted,
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Date: December 10, 2007 By: _____

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